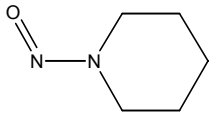
N-NITROSOPIPERIDINE
CAS No. 100-75-4
First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

N-Nitrosopiperidine is *reasonably anticipated to be a human carcinogen* sufficient evidence of carcinogenicity in experimental animals (IARC V.17, 1978; IARC S.7, 1987). When administered in the diet, *N*-nitrosopiperidine induced squamous cell carcinomas of the forestomach, papillomas of the esophagus, hepatocellular adenomas and carcinomas, and liver hemangioendotheliomas in male mice. When administered in drinking water, *N*-nitrosopiperidine induced lung adenomas in mice of both sexes and esophageal carcinomas and hepatocellular carcinomas in rats. When administered orally, *N*-nitrosopiperidine induced hepatocellular carcinomas in monkeys. When administered by subcutaneous injection, the compound induced squamous cell carcinomas and other tumors of the nasal cavity and esophageal squamous cell carcinomas and papillomas in rats and tumors of the nasal cavity, trachea, lung, tongue, palate, esophagus, forestomach, and liver in hamsters. When administered by intraperitoneal injection, *N*-nitrosopiperidine increased the incidence of adenomas of the lung in mice. When administered by intravenous injection, the compound induced carcinomas of the esophagus and pharynx in rats. When administered to pregnant hamsters, a low incidence of tumors of the upper respiratory tract was observed for the offspring and a high incidence of respiratory tract tumors was observed for the mothers.

There are no data available to evaluate the carcinogenicity of *N*-nitrosopiperidine in humans (IARC V.17, 1978, IARC S.7, 1987).

PROPERTIES

N-Nitrosopiperidine is a yellow oil. It is soluble in water, organic solvents, and lipids, and very soluble in acidic solutions. It decomposes in light, and is especially sensitive to ultraviolet light. When heated to decomposition, it emits toxic fumes of nitrogen oxides (NO_x). It is oxidized by strong oxidants to corresponding nitramine. It can be reduced to the corresponding hydrazine and/or amine. It is resistant to hydrolysis.

USE

N-Nitrosopiperidine is used in the production of epoxy resin for electrical leads and for cardiovascular implants. It also has a limited use in cancer research (IARC V.17, 1978). It is used primarily as a research chemical.

PRODUCTION

There is no evidence that *N*-nitrosopiperidine has been manufactured on a commercial scale in the United States (IARC V.17, 1978). One company specializing in laboratory chemicals produces and sells *N*-nitrosopiperidine in 1-, 5-, 10-, and 25-ml quantities (Sigma, 1987). Synthetic production of nitrosamines is limited to small quantities, primarily as research chemicals (HEEP, 1980). The 1979 TSCA Inventory identified one producer of *N*-nitrosopiperidine in 1977 (TSCA, 1979). No production, import, or export data were available.

EXPOSURE

The primary routes of potential human exposure to *N*-nitrosopiperidine are inhalation, ingestion, and dermal contact. Individuals having the highest probability of possible exposure to *N*-nitrosopiperidine are cancer researchers, organic chemists, and workers engaged in the production of epoxy resins. Potential exposure to *N*-nitrosopiperidine during its production is limited because of the small quantities produced. Moreover, nitrosamines decompose rapidly in sunlight and therefore do not persist in ambient air or water (CHIP, 1978). In air it exists solely as a gas (half-life 15 hours).

The general population may possibly be exposed sporadically to low concentrations of *N*-nitrosopiperidine from cigarette smoke and certain foods. Several researchers have reported trace amounts of *N*-nitrosopiperidine in cigarettes, but these observations have not been confirmed in all brands of cigarettes tested. Investigators have detected *N*-nitrosopiperidine concentrations as high as 60 μg/kg in meat and fish products such as bacon, bologna, wieners, and smoked cod; the presence of *N*-nitrosopiperidine in meat, cheese, and spices results from the use of sodium nitrite as a preservative. Also, FDA estimated that between 10,000 and 100,000 patients may be exposed to *N*-nitrosopiperidine because of medical implants, although FDA's Center for Devices and Radiological Health has not taken regulatory action at this time (CHIP, 1978).

N-Nitrosamines are frequently produced during rubber processing and may be present as contaminants in the final rubber products. Potential exposure depends on the ability of the nitrosamines to migrate from the product and enter the body. CPSC and FDA determined that the nitrosamines present in pacifiers and baby bottle nipples can migrate from the pacifier or nipple into saliva, which could result in ingestion of nitrosamines. Significant levels of *N*-nitroso compounds have been identified in a number of materials including pesticides, cosmetics, cutting fluids, and fire-resistant hydraulic fluids. The *N*-nitroso compounds found in these products were apparently formed in situ during storage or handling as the result of a reaction between amines present in the mixture and inorganic nitrite, which may have been added as a corrosion inhibitor (CHIP, 1978).

REGULATIONS

EPA regulates *N*-nitrosopiperidine under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), and Superfund Amendments and Reauthorization Act (SARA). EPA has established a final RQ of 10 lb. *N*-Nitrosopiperidine is subject to report/recordkeeping requirements under RCRA and SARA. FDA regulates *N*-nitrosopiperidine under the Food, Drug, and Cosmetic Act (FD&CA), requiring separate packaging of spices and sodium nitrite in dry premixed cures. This action resulted in a dramatic decrease in the *N*-nitrosopiperidine content of dry mixes. OSHA

regulates *N*-nitrosopiperidine under the Hazard Communication Standard as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-110.